

CLAIMS

5 1) A method for identifying therapeutic
agents for reducing and monitoring the growth, erosion,
rupture or stability of an atherosclerotic plaque
comprising the analysis of the differential expression
of at least two genes coding proteins chosen among
10 among Stearoyl CoA desaturase, Phosphatidic acid
phosphate, and Phosphoinositide-specific-phospholipase-
B1, eventually in association with the analysis of the
differential expression of at least one gene coding a
protein choosen in the group comprising Aldose
15 reductase and aldehyde reductase, Sphingomyelinase,
Acid ceramidase, Ceramide glucosyl transferase,
Sphingosin phosphate liase, Thymosine beta 4, Aldehyde
dehydrogenase, ATPase Ca++ binding protein and CD163

20 2) The method of claim 1, wherein said
analysis is carried out in human or animal cells,
tissue sections or animal models.

25 3) A diagnostic method of artherosclerosis
or cardiovascular disorders relating to the
atherosclerotic plaque in a biological sample of a
subject comprising the analysis of the differential
expression of at least two gene coding a protein chosen
among Stearoyl CoA desaturase, Phosphatidic acid
30 phosphate, and Phosphoinositide-specific-phospholipase-
B1, eventually in association with the analysis of the
differential expression of at least one gene coding a
protein choosen in the group comprising Aldose
reductase and aldehyde reductase, Sphingomyelinase,
Acid ceramidase, Ceramide glucosyl transferase,

Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 Stearoyl CoA deasturase, Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163.

4) The method of claim 3, wherein said analysis is carried out in human cells or tissue sections.

5) The method of any of claims 1 to 4, wherein the analysis is performed at the mRNA or protein level.

6) The method of claims 1 or 3, which comprises :

- providing a plurality of different ligands in the form of an array on a solid surface, said different ligands being complementary to different segments of at least two genes coding a protein chosen among Stearoyl CoA desaturase, Phosphatidic acid phosphate, and Phosphoinositide-specific-phospholipase-B1, and eventually to different segments of at least one gene coding a protein in the group comprising Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 Stearoyl CoA deasturase, Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase

Ca++ binding protein and CD163 or being complementary to different segments of at least one gene coding said proteins,

5 - applying a sample solution potentially containing the targets of the ligands to the array of ligands under conditions which allow the interaction of said ligands and its target, and

 - measuring the interactions of the targets with the different ligands of the array

10 7) The method of claim 6, wherein the ligands are nucleic acid probes and the sample contains target nucleic acids in order to measure the hybridization of the probes with the target nucleic
15 acids.

 8) The method of claim 7, wherein the nucleic acid probes are oligonucleotides.

20 9) The method of claim 8, wherein the array comprises 2 to about 200 oligonucleotides localized in discrete location per square centimeter on the solid surface.

25 10) The method according to any of claims 6 to 9, wherein the sample is from a patient developing arteriosclerotic plaque.

30 11) Method of screening compounds useful for the treatment of arteriosclerosis or cardiovascular disorders relating to the arteriosclerotic plaque comprising the analysis of the differential expression of at least two gene coding a protein chosen among Stearoyl CoA desaturase, Phosphatidic acid phosphate,

and Phosphoinositide-specific-phospholipase-B1, eventually in association with the analysis of the differential expression of at least one gene coding a protein among Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 Stearoyl CoA deasturase, Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 in the presence of a test compound.

12) The method of claim 11, wherein said analysis is carried out in human or animal cells, tissue sections or animal models.

13) The method of any of claims 11 and 12, wherein the analysis is performed at the mRNA or protein level.

14) The method of claim 13, wherein the analysis is performed on a solid support.

15) The method of claim 11, which comprises :

- providing a plurality of different ligands in the form of an array on a solid surface, said different ligands consisting of all or part of at least two gene coding a protein chosen among Stearoyl CoA desaturase, Phosphatidic acid phosphate, and Phosphoinositide-specific-phospholipase-B1, and eventually to all or part of at least one gene coding a

protein among Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 Stearoyl CoA deasturase, Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163.

- applying a solution containing a test compound to the array of ligands, and

- measuring the interaction, such as the binding, of the test compound with the different ligands of the array.

16) The method according to any of claims 1 to 15, wherein the test compound is a protein or molecule of small molecular weight.

17) Method of screening compounds useful for the treatment of artherosclerosis or cardiovascular disorders relating to the atherosclerotic plaque according to any of claims 11 to 13 comprising :

- providing an assay for at least two proteins chosen among Stearoyl CoA desaturase, Phosphatidic acid phosphate, and Phosphoinositide-specific-phospholipase-B1, eventually in association with at least one protein among Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 Stearoyl CoA deasturase, Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl

transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163

5 - contacting said assay with a test compound, and

 - measuring the action of the test compound on the said protein in the assay.

10 18) The method of any of claims 1 to 17, wherein the analysis comprises the measure of the differential expression of at least two genes coding a protein chosen among Stearoyl CoA desaturase, Phosphatidic acid phosphate, and Phosphoinositide-specific-phospholipase-B1, eventually in association
15 with the measure of the differential expression of at least one gene coding a protein among Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163
20 Stearoyl CoA deasturase, Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++
25 binding protein and CD163 and the comparison of said measure with the normal expression of said protein in early and advanced atherosclerotic plaques containing macrophages, under hyperlipidemic conditions and in the absence of high levels of blood glucose and insulin.

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 19) The method of any of claims 1 to 18, wherein the analysis comprises the measure of the differential expression of at least two genes coding a protein chosen among Stearoyl CoA desaturase,

Phosphatidic acid phosphate, and Phosphoinositide-specific-phospholipase-B1, eventually in association with the measure of the differential expression of at least one gene coding a protein among Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 Stearoyl CoA deasturase, Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 and the comparison of said measure with the expression of reference genes that are representative of an atherosclerotic plaque.

20) The method of claim 19, wherein said references gene include membrane associated genes such as CD68, CD36 which are both markers of the macrophage lineage; PECAM 1; a marker for endothelial cells; markers of the inflammatory response such as TLR4, HSP60 and HSP70, Galectin 3 and IL1-R; markers of the oxidative stress including HIF-1 and Paraoxanase 3, metabolic marker such as NADH dehydrogenase; lipoprotein receptors such as LDL-R and VLDL-R.

21) The use of a compound modulating the expression of at least two gene coding a protein chosen among Stearoyl CoA desaturase, Phosphatidic acid phosphate, and Phosphoinositide-specific-phospholipase-B1, and eventually modulating the expression of at least one gene coding a protein among Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin

phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 Stearoyl CoA deasturase, Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, 5 Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca++ binding protein and CD163 or modulating the activity of said at least one protein for the preparation of a pharmaceutical composition useful for preventing and/or 10 treating artherosclerosis or cardiovascular disorders relating to the atherosclerotic plaque.